

# Case Reports

## Hematogenous *Pasteurella multocida* Brain Abscess

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*Pasteurella multocida*, a common cause of infections in animals, is being reported with increasing frequency as a human pathogen.<sup>1</sup> Most infections arise from animal bites and remain localized. More serious deep-seated infections occur occasionally and sometimes involve the central nervous system. There are only five published case reports of brain abscess caused by *P. multocida*, all of which were caused by penetrating trauma or contiguous spread from a suppurative parameningeal focus. We describe the case of a patient with a hematogenously acquired brain abscess caused by *P. multocida*, apparently the first documented case of this type.

### Report of a Case

The patient, a 67-year-old man with mild alcoholic liver disease and severe chronic obstructive pulmonary disease, was admitted to hospital at the Seattle Veterans Administration Medical Center (VAMC) because of a two-day history of headache, sore neck, myalgias, confusion and fever. Before this admission his respiratory illness had necessitated treatment with prednisone, 15 mg a day, continuous supplemental oxygen and bronchodilators. Bronchoscopy and bronchography on three occasions in the past three years for evaluation of a persistent right lower lobe infiltrate on roentgenograms had shown no evidence of malignancy or bronchiectasis. Because of increasingly purulent sputum, he had been receiving ampicillin, 500 mg orally every six hours, for the ten days before hospital admission. The patient had had a pet dog for several years.

On admission the patient's temperature was 40°C (104°F) and his respiratory rate was 28 per minute. Examination of the head, auditory canals and oropharynx disclosed no abnormalities. He had a stiff neck and a positive Kernig's sign. Rales were heard at the right lung base. The findings of cardiac and abdominal examinations were unremarkable and no skin lesions were noted. The patient was confused and lethargic, but the remainder of his neurologic examination showed no abnormalities. The leukocyte count was 30,400 per  $\mu$ l with a predominance of polymorphonuclear cells. A chest x-ray film was unchanged from previous studies. A computed tomographic (CT) scan of the head (without contrast) was normal. Lumbar puncture showed an opening pres-

sure of 285 mm of water and the cerebrospinal fluid specimen contained the following: glucose 80 mg per dl, protein 252 mg per dl, 2,900 leukocytes per  $\mu$ l (80% polymorphonuclear cells) and 11 erythrocytes. Stains and cultures for bacteria, mycobacteria and fungi were negative, as were cryptococcal antigen and counterimmunoelectrophoresis studies. Cultures of urine and blood specimens were sterile; the sputum grew only normal respiratory flora. Following empiric therapy with chloramphenicol, 6 grams given intravenously per day, the patient's fever subsided and he became progressively more alert. On the sixth hospital day a repeat cerebrospinal fluid examination showed only 15 leukocytes (all lymphocytes) and cultures were again negative. Chloramphenicol therapy was discontinued after ten days, and the patient was discharged two weeks after admission, completely recovered neurologically.

Two days after discharge a course of oral ampicillin was begun because of an episode of *Hemophilus influenzae* bronchitis. Five days later he again had headache, stiff neck, fever and progressive confusion. Ten days following his hospital discharge, while en route to the VAMC, he suffered a respiratory arrest. On admission to another hospital he was comatose with a temperature of 40°C (104°F) and a systolic blood pressure of 80 mm of mercury. His neck was rigid and he had unilateral decerebrate posturing. A CT scan of the head showed a 4 by 4 cm right frontal lobe mass and at least four smaller lesions in the right parietal and left and right occipital lobes; all lesions enhanced with contrast (Figure 1). The frontal lobe lesion was drained and a thick abscess wall was removed at craniotomy. Aerobic and anaerobic cultures of an aspirate of the abscess fluid yielded a pure growth of *Pasteurella multocida*, sensitive to all antimicrobials to which it was tested, including ampicillin and chloramphenicol. Blood and urine cultures were negative.

The patient initially received parenteral moxalactam disodium, oxacillin sodium and metronidazole, all of which were later shown to inhibit the *P. multocida* isolate. Therapy was changed to penicillin G only, 12 million units given intravenously per day, when the final culture results were known. The patient was transferred to the Seattle VAMC where, after seven days of steady improvement, he became febrile to 39°C (102°F), tachypneic and obtunded. Another CT scan of the head showed four contrast-enhanced lesions, smaller than those seen seven days previously. Repeat cultures of specimens of the cerebrospinal fluid and blood were negative. Antimicrobial therapy was changed to parenteral nafcillin sodium, 12 grams per day, and moxalactam, 8 grams per day, but the patient remained obtunded and intermittently febrile. Another head CT scan ten days after readmission showed eight to ten abscess cavities (Figure 2). A percutaneous needle aspiration of one of the new abscesses produced fluid that showed rare Gram-positive cocci on Gram's stain, but aerobic and anaerobic cultures were negative. Ultrasound examinations of the abdomen and chest and an echocardiogram failed to reveal a source for the brain abscesses. His condition

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## ABBREVIATIONS USED IN TEXT

CT = computed tomographic

VAMC = Veterans Administration Medical Center

deteriorated and he died six weeks after his second hospital admission.

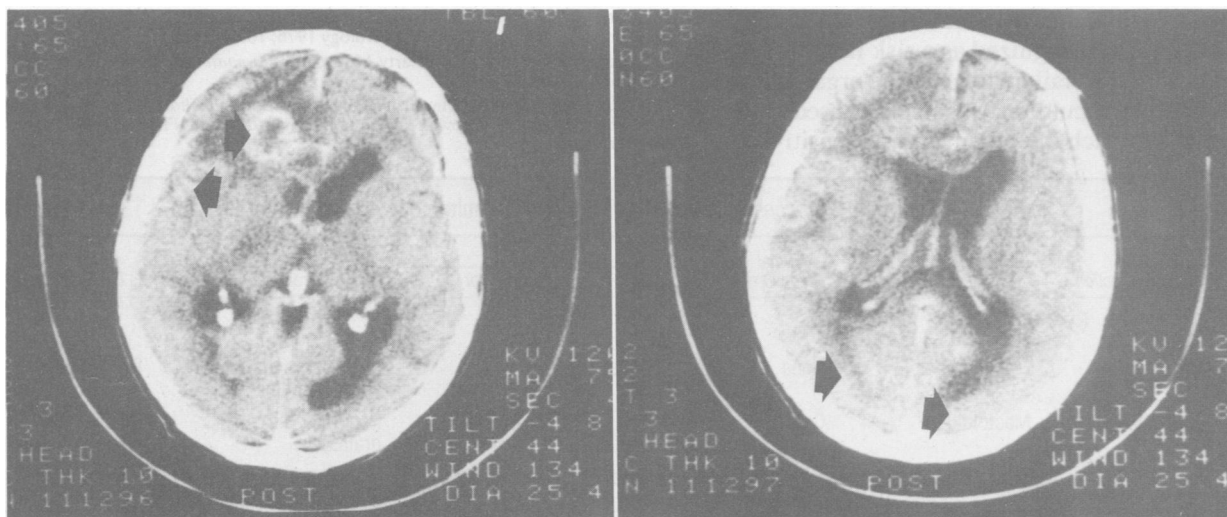
On autopsy examination there were three encapsulated brain abscesses. Tissue Gram's stain of these lesions showed rare Gram-positive cocci but cultures were negative. The right middle and lower lobes of the lungs showed chronic and acute inflammation, but no active infection. No abnormalities were noted in the ears, mastoids or paranasal sinuses, and no other source of infection could be identified.

### Discussion

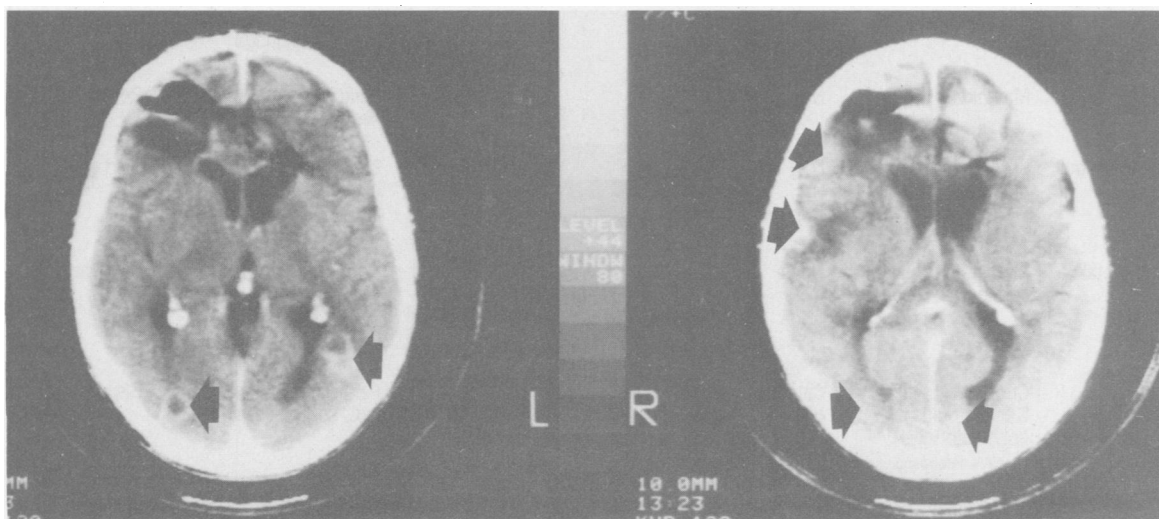
Among the *Pasteurella* species, *P. multocida* is the most frequent human pathogen. It is a small Gram-negative bacillus that grows well on blood but not MacConkey agar; 16 serotypes have been identified, 6 of which are known to cause infections in humans.<sup>2</sup> *P. multocida* is commonly part of the normal respiratory flora of numerous species of mammals and birds.<sup>3</sup> Human respiratory carriage occurs occasionally, usually among healthy people who work with livestock or patients with chronic bronchopulmonary disease who are exposed to household pets harboring the organism.<sup>3,4</sup>

Human disease can be traced to animal exposure in about 75% of all cases<sup>4</sup> but in only about half of those with systemic infections.<sup>3</sup> Patients with chronic pulmonary or liver disease, especially when elderly, seem predisposed to disseminated *P. multocida* infections.<sup>5-10</sup> The spectrum of disease caused by this organism includes infected bite wounds, the most common form of infection<sup>3,11-14</sup>; respiratory disease, including bronchitis, pneumonia, bronchiectasis, lung abscess, empyema and paranasal sinusitis,<sup>15-19</sup> and disseminated disease. At least 49 cases of *P. multocida* bacteremia have been reported.<sup>20,21</sup>

Central nervous system infections with *Pasteurella* species occur infrequently, constituting less than 5% of non-bite-related cases.<sup>4</sup> Meningitis has been the most commonly reported form, with *P. multocida* the predominant species in the 27 documented cases.<sup>20-25</sup> Only five previous cases of brain abscess have been reported, all with *P. multocida* as the infecting organism (Table 1).<sup>26-30</sup> Four of these were due to chronic purulent middle ear and mastoid infections, and one resulted from direct cerebral inoculation by a dog bite. Two cases of intracranial subdural empyema caused by *P. multocida* have also been reported (Table 1). One of the patients was a man with alcoholism who had metastatic carcinoma of the tongue and in whom *P. multocida* bacteremia probably infected a chronic subdural hematoma.<sup>31</sup> The other patient



**Figure 1.**—Computed tomographic scan of the head, with contrast, showing a 4 by 4 cm right frontal lobe abscess and three smaller abscesses (arrows).



**Figure 2.**—Computed tomographic scan of the head, with contrast, taken 19 days after Figure 1, showing several of the 8 to 10 abscess cavities (arrows).

# CASE REPORTS

had chronic paranasal sinusitis and a subdural empyema developed two weeks after an ethmoid polypectomy.<sup>32,33</sup> In four of the five cases that provided the information, exposure to animals (cats or dogs) was reported. In two cases in addition to ours, Gram-positive cocci were grown from or seen on stains of a specimen of the abscess fluid. *P. multocida* grew from other sites (ear drainage, mastoids, pharynx, blood) in four cases and from the responsible animals in two cases. All of the previously reported cases showed a single abscess, unlike in our patient, who had multiple abscesses. Because culture of only one of these lesions was positive, however, the microbial cause of the others is uncertain. All of the patients received both surgical drainage and antibiotics; only two (including our patient) did not recover.

Because most of the cases of meningitis and one of the cases of subdural empyema caused by *P. multocida* were presumably hematogenously acquired, it is not surprising that brain abscess with this bacterium could also occur by this route. In our patient the multiple abscesses and the lack of a contiguous source of infection make the bacteremic route likely, despite the absence of positive blood cultures and the failure of extensive premortem and postmortem investigations to identify a primary source. The initial focus was most likely his chronic pulmonary infection. Such infections are common antecedents to hematogenously acquired brain abscesses, and *P. multocida* is known to infect patients with chronic bronchopulmonary disease.<sup>4</sup> Alcoholic liver disease, which this patient had, is also recognized as a risk factor for *Pasteurella* septicemia.<sup>6,7,14</sup> The failure to grow the organism from several sputum and blood cultures was likely caused by his receiving antibiotics to which the organism was sensitive

before these cultures. Furthermore, a light growth of *P. multocida* in a sputum culture with mixed respiratory flora would likely not have been detected. The finding of rare Gram-positive cocci on both premortem and postmortem Gram's stains of abscess fluid may represent either contamination at the time of the original operation or a true second pathogen. While penicillin is the usual drug of choice for *Pasteurella* infections,<sup>34</sup> the atypical course of our patient's illness, the invasive procedures he underwent and his apparent worsening during therapy led to his receiving broad-spectrum antimicrobial therapy. Why he failed to respond to surgical drainage and appropriate antibiotic coverage is unclear, but his severe underlying illnesses and perhaps corticosteroid-induced immunosuppression may have been partly responsible.

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TABLE 1.—Intracranial Abscesses Caused by *Pasteurella multocida*

Sources, Patient Age (yr), Sex	Site of Infection	Predisposing Factors	Animal Exposure	Cultures		Treatment	Outcome
				CNS*	Other		
<b>Brain Abscesses</b>							
Svendsen, 1947 <sup>26</sup> 18 ♂ . . . . .	Cerebellum	Mastoiditis	None	Pm and anaerobic streptococci		Penicillin, sulfadiazine; surgical drainage	Recovered
Harris et al, 1953 <sup>27</sup> 11 ♀ . . . . .	Cerebellum	Mastoiditis	Cats	Pm—pure growth	Mastoid—pure growth	Penicillin; surgical drainage	Died
Larsen et al, 1969 <sup>28</sup> 14 ♀ . . . . .	Cerebellum	Mastoiditis	NA	Pm—GPC seen, not grown	Ear swab—no Pm	Oxacillin sodium, chloramphenicol, sulfadiazine; surgical drainage	Recovered
Klein and Cohen, 1978 <sup>29</sup> 1½ ♀ . . . . .	Frontoparietal lobe	Cranial dog bite	Dog	Pm—? pure growth	Dog's mouth—Pm present	"Antibiotic therapy"; surgical drainage	Recovered
Whittle and Besser, 1982 <sup>30</sup> 65 ♀ . . . . .	Temporal lobe	Mastoiditis	NA	Pm—pure growth	Ear swab—Pm present	Penicillin, metronidazole; needle aspiration	Recovered
Present case 67 ♂ . . . . .	Frontal, parietal, occipital	Chronic broncho-pulmonary disease	Dog	Pm—pure growth; GPC seen, not grown	No Pm isolated elsewhere	Oxacillin, moxalactam disodium, metronidazole; surgical drainage	Died
<b>Subdural Empyemas</b>							
Khan and Chan, 1981 <sup>31</sup> 62 ♂ . . . . .	Frontoparietal lobe	Metastatic carcinoma; alcoholism	Dogs	Pm—? pure growth	Blood and pharynx—Pm isolated	Ampicillin; surgical drainage	Recovered
Stern et al, 1981 <sup>32</sup> ; Ellner and Correa-Londoño, 1981 <sup>33</sup> 44 ♀ . . . . .	Frontal lobe	Chronic sinusitis; S/P ethmoid polypectomy	Cats and dogs	Pm—? pure growth	Pets' mouth—Pm present	Penicillin, chloramphenicol; surgical drainage	Recovered

CNS = central nervous system, GPC = Gram-positive cocci, NA = information not available, Pm = *Pasteurella multocida*, S/P = following (status post)

\*Specimens for culture were taken from either an intracranial abscess or epidural empyema.

CNS = central nervous system, GPC = Gram-positive cocci, NA = information not available, Pm = *Pasteurella multocida*, S/P = following (status post)

\*Specimens for culture were taken from either an intracranial abscess or epidural empyema.

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## Rhodamine B Ingestion as a Cause of Fluorescent Red Urine

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RHODAMINE B is a compound with various commercial uses, most notably as a dye. Due to their toxic and carcinogenic potential,<sup>1-4</sup> rhodamine derivatives are not utilized as food additives and their use in cosmetics is restricted by the Food and Drug Administration (FDA). Two cases of rhodamine B ingestion were encountered at the University of California, San Diego (UCSD), Medical Center. Rhodamine B was found in food products allegedly purchased from a bakery in Tijuana, Mexico, and ingestion resulted in urine that fluoresced intensely under long-wave ultraviolet light. A report of human ingestion of rhodamine B has not been previously published.

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## Reports of Cases

### Case 1

The patient, a 17-year-old man, arrived at UCSD Medical Center complaining of red urine and left flank pain. He stated that he had been "kneed" in wrestling practice earlier that day. He said he had had no previous episodes of colored urine and did not use any drugs. On abdominal examination there were no abnormalities except for mild tenderness over the left iliac crest. The urine was bright red on examination. Both hematuria and myoglobinuria were excluded by laboratory analysis. Further questioning revealed that he had ingested large amounts of red chili peppers and cranberry juice 24 hours earlier. However, the patient had ingested this food combination on numerous occasions without having red urine. A urine specimen was then sent to the Toxicology Laboratory, UCSD Medical Center, for further analysis. There a series of intensely fluorescent compounds was detected by chromatography of the urine. On further investigation we learned that the patient had purchased "pink-colored" cookies from a bakery in Tijuana, Mexico, and had eaten several of them the previous day. The patient's family subsequently provided a cookie for analysis.

### Case 2

A 25-year-old woman in her third trimester of pregnancy was admitted to UCSD Medical Center for evaluation of a recent seizure episode. Analysis of a specimen of her urine by the Toxicology Laboratory showed intensely fluorescent compounds. The patient said that she had visited Tijuana earlier in the week and had purchased numerous bakery goods there. However, she could not recall whether any of the goods were pink or red.

## Laboratory Analysis

In the Toxicology Laboratory the urine specimens and the cookie showed intense red fluorescence under long-wave ultraviolet light. Thin-layer chromatography for drugs of abuse<sup>5</sup> was done on the urine specimens from case 1 and case 2 and on a methanolic extract of the cookie from case 1. Five fluorescent compounds were noted in each of the urine specimens. Analysis of the cookie extract showed two fluorescent compounds, one of which corresponded to a major compound in the urine using five chromatography systems. Both infrared and ultraviolet-visible spectra for purified commercial rhodamine B and for one of the two compounds found in the cookie were identical. The amount of rhodamine B in the cookie was estimated gravimetrically to be at least 100 mg. Another major compound in the urine had ultraviolet and visible spectra identical to those published for triethylrhodamine, a rhodamine B metabolite.<sup>6,7</sup> The other fluorescent compounds in the urine were conceivably further de-ethylated metabolites of rhodamine B,<sup>4,8</sup> while the other compound in the cookie was either a contaminant or a degradation product of rhodamine.

## Discussion

Rhodamine B ("basic violet 10," "food red 15," "FD&C red 19") is used commercially as a dye, fluorescent paint, analytic reagent and a cosmetic coloring agent.<sup>9</sup> The compound has toxic properties and is considered to be a possible carcinogen.<sup>9</sup> Oral administration to mice and rats is